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(71) Applicant (for all designated States except US):

MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG

DER WISSENSCHAFTEN E.V. [DE/DE]; Berlin (DE).

97 11 3306.1

(72) Inventors; and
(75) Inventors/Applicants (for US only): WANKER, Erich [AT/DE]; Leichhardtstrasse 61, D-14195 Berlin (DE). LEHRACH, Hans [AT/DE]; Lützelsteiner Weg 50, D-14195 Berlin (DE). SCHERZINGER, Eberhard [DE/DE]; Lützelsteiner Weg 52, D-14195 Berlin (DE). BATES, Gillian [GB/GB]; Division of Medical and Molecular Genetics, United Medical and Dental Schools, Guy's Hospital, Guy's Tower, 8th floor, London SE1 9RT (GB).

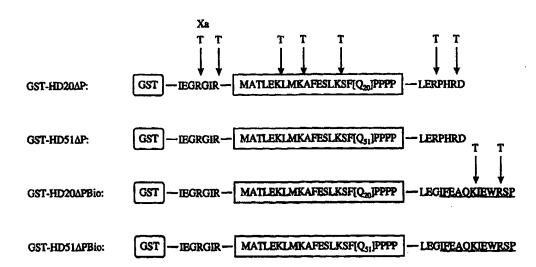
(74) Agent: VOSSIUS & PARTNER; Postfach 86 07 67, D-81634 München (DE).

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(54) Title: COMPOSITION AND METHOD FOR THE DETECTION OF DISEASES ASSOCIATED WITH AMYLOID-LIKE FIBRIL OR PROTEIN AGGREGATE FORMATION



(57) Abstract

The present invention relates to novel compositions useful for elucidating the onset or progress of diseases of preferably neuronal origin associated with the formation of amyloid-like fibrils or protein aggregates. Further, the present invention relates to methods for monitoring said formation as well as to methods for identifying inhibitors of said formation. Additionally, the invention relates to inhibitors identified by the method of the invention as well as to pharmaceutical compositions comprising said inhibitors.

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[DE/DE]; Lützelsteiner Weg 52, D-14195 Berlin (DE). BATES, Gillian [GB/GB]; Division of Medical and Molecular Genetics, United Medical and Dental Schools, Guy's Hospital, Guy's Tower, 8th floor, London SEI 9RT (GB).

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München (DE).

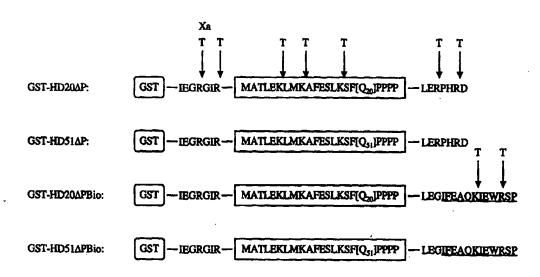
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(54) Title: COMPOSITION AND METHOD FOR THE DETECTION OF DISEASES ASSOCIATED WITH AMYLOID-LIKE FIBRIL OR PROTEIN AGGREGATE FORMATION



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The present invention relates to novel compositions useful for elucidating the onset or progress of diseases of preferably neuronal origin associated with the formation of amyloid-like fibrils or protein aggregates. Further, the present invention relates to methods for monitoring said formation as well as to methods for identifying inhibitors of said formation. Additionally, the invention relates to inhibitors identified by the method of the invention as well as to pharmaceutical compositions comprising said inhibitors.

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INTERNATIONAL SEARCH REPORT

Interns al Application No
PCT/FP 98/04811

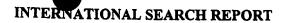
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A. CLASS IPC 6	IFICATION OF SUBJECT MATTER C07K14/47 C12N15/12 C12N15 A01K67/027 A61K48/00	/62 C07K16/I	18 C12	N15/63
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B. FIELDS	SEARCHED			
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Documenta	tion searched other than minimum documentation to the extent the	at such documents are includ	ded in the fields s	searched
Electronic	lata base consulted during the international search (name of data	base and, where practical, s	search terms use	d)
	ENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where appropriate, of the	relevant passages		Relevant to claim No.
X	WO 97 17445 A (CENTRE NAT RECH ; INST NAT SANTE RECH MED) 15 M; see page 3, line 7 - page 4, line see page 14, line 10 - page 16, example 1	ay 1997 ne 33		1,13,20
X	C.A. GUTEKUNST ET AL., : "Identand localization of huntingtin and human lymphoblastoid cell lianti-fusion protein antibodies PROCEEDINGS OF THE NATIONAL ACAUSCIENCES, vol. 92, 1995, pages 8710-8714, XP002101176 cited in the application see page 8710	in brain ines with ' DEMY OF		1-6,8,13
		-/		,
X Furth	er documents are listed in the continuation of box C.	X Patent family me	embers are listed	in annex.
° Special cat	egories of cited documents :	1770 A.A. A. A		
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Internat | Application No PCT/EP 98/04811

Category °	Citation of document, with indication, where appropriate, of the relevant passages	I Batawara a sa
Juliagory .	Onclined of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TROTTIER Y ET AL: "POLYGLUTAMINE EXPANSION AS A PATHOLOGICAL EPITOPE IN HUNTINGTON'S DISEASE AND FOUR DOMINANT CEREBELLAR ATAXIAS" NATURE, vol. 378, no. 6555, 23 November 1995, pages 403-406, XP002009617 see the whole document andspecially last paragraph	1-6,13
X	M.F. PERUTZ: "Glutamine repeats and inherited neurodegenerative diseases: molecular aspects." CURRENT OPINION IN STRUCTURAL BIOLOGY, vol. 6, 1996, pages 848-858, XP002101177 cited in the application see the whole documentbut specially pages 853-856	1-6,8, 14,15
X	L. MANGIARINI ET AL., : "Exon 1 of the HD gene with an expanded CAG repeat is sufficient to cause a progressive neurological phenotype in transgenic mice" CELL, vol. 87, 1996, pages 493-506, XP002101178 cited in the application see the whole document	2-6,23
A	WO 95 29243 A (UPJOHN CO) 2 November 1995 see page 7, line 18 - page 11, line 30	1,8,15
A	EP 0 293 249 A (AMRAD CORP LTD) 30 November 1988 see abstract see page 2, column 2, line 40 - page 3, column 3, line 48 see page 8, column 13, line 36-51	1,8,15
A -	K. STOTT ET AL.,: "Incorporation of glutamine repeats makes protein oligomerize: implications for neurodegenerative diseases" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, 1995, pages 6509-6513, XP002101179 cited in the application see the whole document	1,2,6,8
	cited in the application see the whole document	





Internat | Application No PCT/EP | 98/04811

X WO 96 28471 A (PHARM PEPTIDES INC) 19 September 1996 see abstract see page 3, line 5 - page 6, line 5 see page 7, line 10-26 see page 48, line 21 - page 53, line 15; examples 1,2 X MERLINI ET AL.,: "Interaction of the anthracycline 4'-10do-4'-deoxydoxorubicin with amyloid fibrils: inhibition of amyloidognesis" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, 1995, pages 2959-2963, XP002101180 see the whole document X KISILEVSKI ET AL.,: "Arresting anyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547 see the whole document P,X DATABASE WPI Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRITTMATTER WARREN J ET AL) 3 March 1998 see the whole document	WO 96 28471 A (PHARM PEPTIDES INC) 19 September 1996 see abstract see page 3, line 5 - page 6, line 5 see page 7, line 10-26 see page 48, line 21 - page 53, line 15; examples 1,2 X MERLINI ET AL.,: "Interaction of the anthracycline 4'-idod-4'-deoxydoxorubicin with amyloid fibrils: inhibition of amyloidogenesis" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, 1995, pages 2959-2963, XP002101180 see the whole document X KISILEVSKI ET AL.,: "Arresting amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547 see the whole document P,X DATABASE WPI Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & Wo 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRITMATTER WARREN J ET AL) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application	Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	10.0
19 September 1996 see abstract see page 3, line 5 - page 6, line 5 see page 7, line 10-26 see page 48, line 21 - page 53, line 15; examples 1,2 MERLINI ET AL: "Interaction of the anthracycline 4'-1odo-4'-deoxydoxorubicin with amyloid fibrils: inhibition of amyloidogenesis" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, 1995, pages 2959-2963, XP002101180 see the whole document KISILEVSKI ET AL.,: "Arresting amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547 see the whole document P,X DATABASE WPI Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRITTMATTER WARREN J ET AL) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application	19 September 1996 see abstract see page 3, line 5 - page 6, line 5 see page 7, line 10-26 see page 48, line 21 - page 53, line 15; examples 1,2 MERLINI ET AL.,: "Interaction of the anthracycline 4'-lodo-4'-deoxydoxorubicin with amyloid fibrils: inhibition of amyloidogenesis" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, 1995, pages 2959-2963, XP002101180 see the whole document KISILEVSKI ET AL.,: "Arresting amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547 see the whole document P,X DATABASE WPI Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application see the whole document		Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
anthracycline 4'-1odo-4'-deoxydoxorubicin with amyloid fibrils: inhibition of amyloidogenesis" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, 1995, pages 2959-2963, XP002101180 see the whole document X KISILEVSKI ET AL.,: "Arresting amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547 see the whole document P,X DATABASE WPI Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRIITMATTER WARREN J ET AL) 3 March 1998 see the whole document P,X E SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application	anthracycline 4'-1odo-4'-deoxydoxorubicin with amyloid fibrils: inhibition of amyloidogenesis" PROCEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, 1995, pages 2959-2963, XP002i01180 see the whole document X KISILEVSKI ET AL.,: "Arresting amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547 see the whole document P,X DATABASE WPI Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRITTMATTER WARREN J ET AL) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application see the whole document	X	19 September 1996 see abstract see page 3, line 5 - page 6, line 5 see page 7, line 10-26 see page 48, line 21 - page 53, line 15;	20-22
amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547 see the whole document P,X DATABASE WPI Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRITTMATTER WARREN J ET AL.) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application	amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547 see the whole document P,X DATABASE WPI Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRITTMATTER WARREN J ET 20-22 AL) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application see the whole document	X	anthracycline 4'-1odo-4'-deoxydoxorubicin with amyloid fibrils: inhibition of amyloidogenesis" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, 1995, pages 2959-2963, XP002101180	20-22
Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRITTMATTER WARREN J ET AL.) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application	Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998 see abstract P,X US 5 723 301 A (STRITTMATTER WARREN J ET AL) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application see the whole document	X	amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer disease" NATURE MEDICINE, vol. 1, no. 2, 1995, pages 143-148, XP000611547	20-22
AL) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application	AL) 3 March 1998 see the whole document P,X E. SCHERZINGER ET AL.,: "Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application see the whole document	Ρ,Χ	Week 9824 Derwent Publications Ltd., London, GB; AN 98-272215 XP002101183 & WO 98 18920 A (SRL INC.), 7 May 1998	
"Huntingtin-encoded polyglutamine 8-12, expansions from amyloid-like protein aggregates in vitro and in vivo" 20,22,23 CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application	"Huntingtin-encoded polyglutamine 8-12, expansions from amyloid-like protein 15-18 aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application see the whole document ——	Р,Х	AL) 3 March 1998	20-22
	-/	Ρ,Χ	"Huntingtin-encoded polyglutamine expansions from amyloid-like protein aggregates in vitro and in vivo" CELL, vol. 90, 8 August 1997, pages 549-558, XP002101181 cited in the application	8-12, 15-18,





Internati | Application No PCT/EP 98/04811

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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	·	
Category °	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
Р,Х	S.W. DAVIES ET AL.,: "Formation of nuronal intrnuclear inclusions underlies the neurological dysfunction in mice transgenic for the HD mutation" CELL, vol. 90, 8 August 1997, pages 537-548, XP002101182 cited in the application see page 539, discussion and page 546.		1-6,13, 23
	·		



Information on patent family members

Interna' if Application No PCT/EP 98/04811

Patent document cited in search report		Publication date	Patent family member(s)		Publication date	
WO	9717445	Α	15-05-1997	FR	2741088 A	16-05-1997
WO	9529243	Α	02-11-1995	AU	2355895 A	16-11-1995
				EP	0758393 A	19-02-1997
				JP	9512426 T	16-12-1997
EP	0293249	Α	30-11-1988	AT	79902 T	15-09-1992
				AU	607511 B	07-03-1991
				AU	1793288 A	21-12-1988
				WO	8809372 A	01-12-1988
				CA	1338903 A	11-02-1997
				DE	3873989 A	01-10-1992
				DK	38189 A	27-01-1989
				ES	2045115 T	16-01-1994
				GR	3006173 T	21-06-1993
				JP	6081596 B	19-10-1994
				JP	1503441 T	22-11-1989
			•	NO	178894 B	18-03-1996
				US	5654176 A	05-08-1997
WO	9628471	Α	19-09-1996	US	5817626 A	06-10-1998
				US	5854215 A	29-12-1998
				AU	5252496 A	02-10-1996
				CA	2214247 A	19-09-1996
				EP	0815134 A	07-01-1998
				US	5854204 A	29-12-1998
US	5723301	A	03-03-1998	NONE		